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FORMULATION DEVELOPMENT AND EVALUATION OF ORODISPERSIBLE TABLET OF DICLOFENAC SODIUM BY SUBLIMATION TECHNIQUE

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ABSTRACT

The purpose of this investigation was to develop fast dissolving tablets of diclofenac sodium using camphor as a subliming agent. Orodispersible tablets of diclofenac were prepared by wet granulation technique using Camphor as subliming agent and Sodium starch glycolate together with crosscarmellose sodium as superdisintegrants. Camphor was sublimed from the granules by exposing the granules to vacuum. The porous granules were then compressed into tablets. Alternatively, tablets were first prepared and later to vacuum. The formulations were evaluated for Disintegration time, In Vitro dissolution, hardness, friability, weight variation and thickness.

KEYWORDS: Mouth dissolving tablet. Diclofenac, Subliming agent, Super disintegrant, Camphor.

INTRODUCTION

The tablet is the most widely used dosage form because of its convenience in terms of self-administration, compactness, and ease in manufacturing. However, geriatric and pediatric patients experience difficulty in swallowing conventional tablets.[1] Paediatric and geriatric patients may have difficulties in swallowing or chewing pharmaceutical dosage forms after oral administration. Tablets that rapidly dissolve upon contact with saliva in the buccal cavity could present a solution to these problems and so there is an increased interest in characterize orally disintegrating tablets dosage forms for buccal, sublingual and oral administration.[2]

Orodispersible tablet is uncoated tablet intended to be placed in the mouth where they disperse rapidly before being swallowed". Disintegrate within 3 min when examined by the

test for disintegration of tablet.[3]

Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down the stomach. In such cases the bioavailability is greater than those observed for conventional dosage form. ODT dosage form disintegrate in patient's mouth within few seconds without need of water, or chewing, providing best remedy for the patient suffering from dysphasia. The European Pharmacopoeia defined ODT as a tablet that to be placed in the mouth where it disperses rapidly before swallowing in less than 3 minutes. United States of America food and drug administration (FDA) defines oral dispersible tablet (ODT) as "A solid dosage form containing medicinal substances (or) active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon a tongue". Mouth dissolving tablet system can be defined as a tablet that disintegrates and dissolves rapidly in saliva within few seconds without need of drinking water or chewing. In spite of tremendous development in drug delivery technology, oral route remains perfect route for administration of therapeutic reagents because of low cost of therapy, ease of administration, accurate dose, self-medication, pain avoidance, leading to high level of patient compliance. Tablets and capsules are the most popular dosage forms but main drawback of such dosage forms is dysphasia or difficulty in swallowing. This problem led to development of novel solid dosage forms such as mouth dissolving tablets that disintegrate and dissolve rapidly in saliva without need of water. Mouth dissolving tablets avoid first pass metabolism and enhance bioavailability of active ingredient. Novel ODT technologies address many patient and pharmaceutical needs such as enhanced life cycle management to convenient dosing particularly for pediatric, geriatric & psychiatric patients who have difficulty in swallowing (Dysphagia) conventional tablet & capsules. Oro-dispersible tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people who are busy in travelling & may not have access to water.

IDEAL PROPERTIES OF ORALLY FAST DISSOLVING TABLETS[4]

1. Drug and dosage form stability.
2. Mechanical strength of final product.
3. Taste, good mouth feel.
4. Rate of absorption from the saliva solution.
5. Overall bioavailability.
6. Require no water for oral administration.

7. Have a pleasing mouth feel.
8. Have an acceptable taste masking property.
9. Be harder and less friable.

❖ TECHNIQUES USED IN THE PREPARATION OF ORALLY DISINTEGRATING TABLETS (ODTS)[5]

a) Molding.
b) Freeze drying.
c) Sublimation.
d) Spray-Drying.
e) Mass-Extrusion.
f) Direct compression.
g) Phase transition.

❖ PATENTED TECHNOLOGIES FOR ODTS[6]

a) Zydis Technology.
b) Durasolv Technology.
c) Orasolv Technology.
d) Flash Dose Technology.
e) Wow tab Technology.
f) Flash tab Technology.

ADVANTAGES OF ODTS[7]

1. Ease of administration to patients who refuse to swallow a tablet, such as pediatric.
2. Convenience of administration and accurate dosing as compared to liquids.
3. Rapid dissolution of drug and absorption which may produce rapid, onset of action.
4. No need of water to swallow the tablet.
5. Can be easily administered to pediatric, elderly and mentally disabled patients.
6. Suitable for sustained/controlled release actives.
7. Allows high drug loading.
8. Dissolution and absorption of drug is fast, offering rapid onset of action.
9. Bioavailability of drugs is increased as some drugs are
10. Absorbed from mouth, pharynx and esophagus through saliva

LIMITATIONS OF ODTS[8]

1) Drugs with relatively large doses are difficult to formulate into ODTs.
2) Patients who concurrently take anti-cholinergic medications may not be the best candidates for ODTs.
3) Tablet usually have insufficient mechanical strength. Hence, it requires careful packaging and handling.
4) Tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly.
5) They are more susceptible to degradation by humidity and temperature.

PREPARATION OF ORODISPERSIBLE TABLETS BY SUBLIMATION METHOD

Diclofenac sodium tablets were prepared by sublimation technique. The basic principle involved in preparing orodispersible tablets by sublimation technique is inert solid ingredients (E.g. camphor) is added to other tablet excipients and the blend is compressed into tablet. Removal of volatile material by sublimation generated a porous structure. A compressed tablet containing mannitol and camphor is prepared by sublimation technique. The tablets dissolve within few seconds and exhibit sufficient mechanical strength for practical use.

MATERIAL AND METHODOLOGY[9]

Preparation of ODT by sublimation

The orodispersible tablets of Diclofenac sodium were prepared using the subliming agent, camphor, sodium starch glycolate and cross carmellose sodium as superdisintegrants, mannitol as a diluent, sodium saccharin as sweetening agent, alcoholic solution of PVP (10%w/v) as binder and magnesium stearate as a flow promoter. The composition of the each batch shown in Table 1.

Table 1: Composition of different batches of ODTs of Diclofenac sodium[10]

Ingredients (mg)	F1	F2	F3	F4
Diclofenac sodium	100	100	100	100
Camphor	--	--	12.5	12.5
Sodium Saccharine	2.5	2.5	2.5	2.5
crosscarmellose sodium	--	15	--	15
sodium starch glycolate	15	--	15	--
Magnesium stearate	2.5	2.5	2.5	2.5
Mannitol (q.s)	250	250	250	250

All batches were prepared by using 10% polyvinylpyrrolidone in ethyl alcohol as a binder and 1% magnesium stearate. Camphor was sublimed from granules in Batches F3 and from tablets in Batch F4. The raw materials were passed through a 100-mesh screen prior to mixing. The drug and other ingredients were mixed together, and a sufficient quantity of alcoholic solution of PVP (10%w/v) was added and mixed to form a coherent mass. The wet mass was granulated using sieve no. 12 and regranulated after drying through sieve no. 16. Granules of the formulations containing either of the superdisintegrants but without camphor (F1 and F2) were dried in a tray dryer at 60^0 C for 30 min. resulting in localized drying. Other granular formulations (F3 to F4) contained a subliming agent and were dried at room temperature, 20- 22 ^{0} C for 8hrs. During drying, the camphor sublimed with the formation of a porous structure on the surface of the tablet. The dried granules were then blended with talc, magnesium stearate and compressed into tablets using 8- station rotary tablet compression machine (A Jaguar JMD 4-8). Sublimation was performed from tablets instead of granules at 60º C in selected batch (F4).

EVALUATION OF FORMULATED TABLETS[11]

HARDNESS[4]

The crushing strength of the tablets was measured using a Pfizer tablet hardness tester (Omega Scientific Industries, Mumbai, India). Three tablets from each formulation batch were tested randomly and the average reading noted.

FRIABILITY[8]

Twenty tablets were weighed and placed in a Roche friabilator (Electrolab, India). The tablets were rotated at 25 rpm for 4 min. The tablets were then dedusted and reweighed and the percentage of weight loss was calculated. The percentage friability of the tablets was measured as per the following formula,

$$\% \text{ Friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

WEIGHT VARIATION[3]

Randomly, twenty tablets were selected after compression and the mean weight was determined.

None of the tablets deviated from the average weight by more than ±7.5% (USPXX).

THICKNESS[4]

Thickness of tablet was determined by using digital venire caliper (Aero Space).

RESULT AND DISCUSSION

The ODTs of Diclofenac sodium were successfully prepared and evaluated. Hardness of the formulated batches was found to be in the range of 3.7 ±0.42 (F2) to 4.7 ± 0.63 kg/cm^2 (F4). The friability of the ODT was within the acceptable limits. All the batches complied the friability test. The disintegration time of the formulated batches was found to be in the range of 43 sec (F4) to 185 sec (F1). Higher DT for batches F1 & F2 was due to the absence of subliming agent, camphor in these batches where their porosity was less. Batches F3 & F4 contained camphor as the subliming agent, hence these batches had higher porosity and showed lesser disintegration time of 75 sec & 43 sec respectively.

Table 2: Evaluation of ODTs of Diclofenac sodium

Formulation	Hardness (kg/cm^2) n=3	Friability (%) n=3	Disintegration Time (Sec)	Thickness
F1	4.2 ±1.6	0.48%	185	4.60mm
F2	3.7 ±0.42	0.38%	162	4.57mm
F3	3.8 ±1.4	0.26%	75	4.58mm
F4	4.7 ± 0.63	0.13%	43	4.60mm

CONCLUSION

From above results it can be concluded that formulation Batch F4 showed less Disintegration time (43 sec) due to use of subliming agent camphor. When camphor sublimes it created pores on tablet surface so, dissolution fluid easily penetrates inside tablet. Also Hardness of tablet has been improved due to melting of camphor leads to bonding formation in tablet.

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